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| 10/519,259 | 02/14/2006 | Michael Schutz | DEBE:046US/10413939 | 3637 |

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| EXAMINER | |
|---|---|
| TSAY, MARSHA M | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/519,259 | SCHUTZ ET AL. | |
| | Examiner | Art Unit | |
| | Marsha M. Tsay | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 11, 2008 has been entered.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claim 6 is canceled. Claims 1-5, 7-18 are pending and currently under examination.

Priority: The request for priority to GERMAN 103 07 793.6, filed February 24, 2003, and GERMAN 102 28 133.5, filed June 24, 2002, are acknowledged.

**Objections and Rejections**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-12, 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4 recite p12-similar bacteriophage tail protein. The claims have been amended to recite that the bacteriophage tail protein binds to the core region of endotoxin, which defines that "similar" means at least the retention of the p12 phage tail protein function. However, while

a definition for the function of "p12-similar" has been provided, Applicants have not defined the structure of "p12-similar."

Claims 2-3, 5, 7-12, 14-17 are included in this rejection because they are dependent on the above claims and fail to cure the defect.

The reason for maintaining the rejection of claims 1-5, 7-12, 14-17 as indefinite is noted above.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 11, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (1999 Virus Research 60: 95-99; previously cited). For examination purposes, "p-12 similar" has been given its broadest meaning and can encompass any bacteriophage tail protein.

Suzuki et al. disclose the specific interaction of fused H protein of bacteriophage ϕX174 with receptor lipopolysaccharides (LPS). Various concentrations of HisH (histidine-tagged H protein) were adsorbed onto 96 flat-bottom wells, rinsed, and incubated with a sample of biotinylated LPS (p. 97 col. 2; claims 1, 11). The wells were washed to remove unbound LPS, and then added with streptavidin-peroxidase complex (p. 98 col. 1; claims 2). The bound biotinylated LPSs were detected at absorbance of 490 nm (p. 98 Fig. 3; claims 2-3, 15). In Figure 3, Suzuki et al. teach the dose-dependent binding of biotinylated LPS from *E. coli* to

HisH (histidine-tagged H protein) (p. 98; claims 1, 3, 11, 15). Suzuki et al. disclose a first assay measuring phage ϕX174 activity of biotinylated LPSs were incubated in Tris-HCl buffer, NaCl, $MgSO_4$, and $CaCl_2$ with the biotinylated LPSs (p. 97 col. 2). Suzuki et al. do not explicitly teach His-tagged phage ϕX174 is incubated with divalent ions with LPSs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the buffer system including Tris-HCl buffer, NaCl, $MgSO_4$, and $CaCl_2$, used in the first assay for the second assay measuring the interaction of His-tagged phage ϕX174 with biotinylated LPSs because both assays involve measuring the interaction of the same phage protein with biotinylated LPSs (claims 1-4, 11, 15) because it is known in the art that calcium and magnesium bind proteins and both phage ϕX174 and His-tagged phage ϕX174 are equivalent proteins. One of ordinary skill would further recognize that different carriers can be used to immobilize the phage protein in an assay system for measuring the interaction between said phage protein and LPS (claim 4).

Applicants have currently amended claims 1 and 4 to recite that the bacteriophage tail protein binds to the core region of endotoxin, which defines that "similar" means at least the retention of the p12 phage tail protein function.

Applicants also assert (1) Suzuki et al. neither teach the detection of endotoxin nor the removal of endotoxin as presently claimed. The intent of their work was "to prepare H protein using genetic engineering techniques and examine whether H protein could, by itself, recognizes the receptor LPS" (Suzuki et al. p. 96, 2nd paragraph). (2) ϕX174 is a phage that is specific for "rough mutants" (Suzuki et al. p. 95 introduction; p. 98 right column). These are special mutants

with a shortened version of LPS (no O-antigen) often found in less pathogenic laboratory bacterial strains, but the common and more pathogenic bacterial strains exhibit "smooth LPS," which is not even recognized by the H protein of ϕX174 (Suzuki et al. p. 98 right column). (3) Suzuki et al. do not use the His-tag as a coupling group like as in present claim 11, but only as a vehicle to facilitate protein purification (Suzuki et al. p. 97 1st paragraph). (4) The phage protein was merely adsorbed to the microtiter plates, and not immobilized by coupling groups as in present claim 11. (5) The LPS-labeled with biotin is directly detected in Suzuki et al. via a streptavidin-peroxidase complex (pages 97-98), whereas the "marked endotoxin" of present claim 15 is used as a tool to detect the sample endotoxin to be detected in a competitive assay. Applicant's arguments have been fully considered but they are not persuasive.

(1) Suzuki et al. disclose that the fused H protein of bacteriophage ϕX174 interacts with biotinylated LPS. Therefore, even if not explicitly disclosed by Suzuki et al., it would be reasonable for one of ordinary skill to understand that fused H protein of bacteriophage ϕX174 would naturally detect biotinylated LPS first before interacting with said LPS. Further, it would also be reasonable for one of ordinary skill to recognize that once said fused H protein of bacteriophage ϕX174 has interacted with said LPS, the bound LPS could be removed and/or isolated from other molecules in a sample.

(2) Suzuki et al. disclose that said fused H protein of bacteriophage ϕX174 binds to the R-core region of the biotinylated LPS. It is known in the art that the endotoxin complex consists of three components, an outer O-polysaccharide coat, a middle portion (the R-core), and an inner A lipid coat (as evidenced by Gianella p. 3). Therefore, regardless of the type of LPS that is recognized by fused H protein of bacteriophage ϕX174, the ϕX174 of Suzuki et al. recognizes

and binds to the core region of endotoxin, therefore, meeting the p12-similar phage tail protein function.

Regarding points (3), (4), and (5), while the purpose of the His-tag and labeled-LPS used in the instant process may be different than the His-tag and "marked endotoxin" used in Suzuki et al. (i.e., protein purification and detection of labeled-LPS through a streptavidin-peroxidase complex), it does not alter the conclusion that its use in the prior art would have been obvious from the purpose disclosed in the references. The prior art can suggest the same modification or combination to solve a different problem or achieve a different advantage. [see also MPEP 2144]. In this instance, Suzuki et al. disclose a method of detecting biotinylated-LPS comprising using a bacteriophage tail protein comprising a His-tag.

Regarding Applicants' assertion that the phage protein of Suzuki et al. was merely adsorbed to the microtiter plates, and not immobilized by coupling groups as in present claim 4, it would have been obvious to one of ordinary skill to recognize that adsorbing said protein onto a surface would be functionally equivalent to immobilizing said protein by a coupling group since both techniques would result in an "immobilized" protein. One of ordinary skill would recognize that different steps for performing a protein assay can be improved upon and substituted, one for the other, if said steps are functionally equivalent to each other.

For these reasons, claims 1-4, 11, 15 remain rejected under 35 U.S.C. 103(a).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 13-16, 18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-28 of copending Application No. 10583415 ('415). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the '415 claims are both drawn to a method for detecting endotoxin comprising the steps of incubating a sample with bacteriophage tail proteins immobilized on a surface, and removing and/or detecting the phage tail protein-endotoxin complex by spectroscopic means.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

August 26, 2008